A novel hybrid CRISPR tool for gene network perturbation and hiPSC engineering

Grant Award Details

A novel hybrid CRISPR tool for gene network perturbation and hiPSC engineering

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-12669

Project Objective: To develop a novel CRISPR-based technology that enables the simultaneous up- and downregulation of multiple genes in hiPSC, validate the tool by differentiating hiPSC into cardiomyocytes with greater precision and purity than achieved by current gold standard methods, and to share the tool with the research community.

Investigator:

Name:	Stanley Qi
Institution:	Stanford University
Type:	PI

Disease Focus: Heart Disease

Human Stem Cell Use: iPS Cell

Award Value: $704,661

Status: Pre-Active

Grant Application Details

Application Title: A novel hybrid CRISPR tool for gene network perturbation and hiPSC engineering

Public Abstract:

Research Objective

A CRISPR-based tool for simultaneous up- and downregulation of many (~5-20) genes, and a computational tool using scRNA-seq data to predict which genes to perturb for efficacious cell-type conversion.

Impact

A critical bottleneck to the creation of specific cell types from stem cells (and related therapies) is our current inability to make cells execute complex multi-gene programs on command.

Major Proposed Activities

- Develop and characterize a hybrid CRISPR array system for simultaneous up- and downregulation.
- Readout of multi-gene perturbation with single-cell RNA sequencing.
- Development of a machine-learning computational model for predicting target genes for multi-gene regulation.
- Direct hiPSCs into a mesodermal progenitor state using simultaneous perturbation of multiple genes.
- Direct hiPSCs into a mature cardiomyocyte state using simultaneous perturbation of multiple genes.

Statement of Benefit to California:

This research will lead to the creation of a novel CRISPR-based platform technology to enable the creation of diverse engineered cell types for many applications. These tools can be used to advance understanding of specific cell types and to develop therapeutics that can help Californians. In addition, we will create stem cell lines derived from donors of diverse races, ages, and sexes. This will allow for more personalized therapeutics for underserved populations of California.
